Claims

1. A method of identifying a subject predisposed to a disorder associated with ion channel dysfunction, comprising ascertaining whether at least one of the genes encoding ion channel subunits in said subject has undergone a mutation event selected from the group consisting of the mutation events set forth in the following Table:

Subunit Gene	Exon/Intron	DNA Mutation
SCN1A	Exon 5	c664C→T
SCN1A	Exon 8	c1152G→A
SCN1A	Exon 9	c1183G→C
SCN1A	Exon 9	c1207T→C
SCN1A	Exon 9	c1237T→A
SCN1A	Exon 9	c1265T→A
SCN1A	Exon 21	c4219C→T
SCN1A	Exon 26	c5339T→C
SCN1A	Exon 26	c5674C→T
SCN1B	Exon 3	c254G→A
SCN2A	Exon 6A	c668G→A
SCN2A	Exon 16	c2674G→A
SCN2A	Exon 17	c3007C→A
SCN2A	Exon 19	c3598A→G
SCN2A	Exon 20	c3856G→A
SCN2A	Exon 12	c1785T→C
SCN2A	Exon 27	c4919T→A
SCN1A	Intron 9	IVS9-1G→A
SCN1A	Intron 23	IVS23+33G→A
SCN2A	Intron 7	IVS7+61T→A
SCN2A	Intron 19	IVS19-55A→G
SCN2A	Intron 22	IVS22-31A→G
SCN2A	Intron 2	IVS2-28G→A
SCN2A	Intron 8	IVS8-3T→C
SCN2A	Intron 11	IVS11+49A→G
SCN2A	Intron 11	IVS11-16C→T
SCN2A	Intron 17	IVS17-71C→T
SCN2A	Intron 17	IVS17-74delG
SCN2A	Intron 17	IVS17-74insG
CHRNA5	Exon 4	c400G→A
CHRNA2	Exon 4	c373G→A
CHRNA3	Exon 2	c110G→A
CHRNA2	Exon 4	c351C→T

CHRNA2	Exon 5	c771C→T
CHRNA3	Exon 2	c159A→G
CHRNA3	Exon 4	c291G→A
CHRNA3	Exon 4	c345G→A
CHRNA2	Intron 3	IVS3-16C→T
CHRNA3	Intron 3	IVS3-5T→C
CHRNA3	Intron 4	IVS4+8G→C
KCNQ2	Exon 1	c204-c205insC
KCNQ2	Exon 1	c1A→G
KCNQ2	Exon 1	c2T→C
KCNQ2	Exon 8	c1057C→G
KCNQ2	Exon 11	c1288C→T
KCNQ2	Exon 14	c1710A→T
KCNQ2	Exon 15	c1856T→G
KCNQ2	Intron 9	IVS9+(46-48)delCCT
KCNQ3	Intron 11	IVS11+43G→A
KCNQ3	Intron 12	IVS12+29G→A
GABRB1	Exon 5	c508C→T
GABRB1	Exon 9	c1329G→A
GABRB1	Exon 8	c975C→T
GABRG3	Exon 8	c995T→C
GABRA1	5′ UTR	c-142A→G
GABRA1	5′ UTR	c-31C→T
GABRA2	3′ UTR	c1615G→A
GABRA5	5′ UTR	c-271G→C
GABRA5	5′ UTR	c-228A→G
GABRA5	5′ UTR	c-149G→C
GABRB2	5′ UTR	c-159C→T
GABRB2	3′ UTR	c1749C→T
GABRPi	5′ UTR	c-101C→T
GABRB1	Intron 1	IVS1+24T→G
GABRB1	Intron 6	IVS6+72T→G
GABRB1	Intron 7	IVS7-34A→G
GABRB3	Intron 1	IVS1-14C→T
GABRB3	Intron 7	IVS7+58delAA
GABRD	Intron 6	IVS6+132insC
GABRD	Intron 6	IVS6+130insC
GABRD	Intron 6	IVS6+73delCGCGCCCACCGCCCCTTCCGCG
GABRG3	Intron 8	IVS8-102C→T

2. A method as claimed in claim 1 wherein a cDNA derived from said subject comprises the sequence set forth in one of SEQ ID NOS: 1-72.

3. A method as claimed in claim 1 wherein a cDNA derived from said subject has the sequence set forth in one of SEQ ID NOS: 1-72.

4. A method as claimed in any one of claims 1 to 3, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype in said subject.

5. A method as claimed in any one of claims 1 to 3, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness in said subject.

6. A method as claimed in any one of claims 1 to 3, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.

7. A method as claimed in any one of claims 1 to 3, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia,

myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness, when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.

8. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit wherein a mutation event selected from the group consisting of the mutation events set forth in the following Table:

Subunit Gene	Exon/Intron	DNA Mutation
SCN1A	Exon 5	c664C→T
SCN1A	Exon 8	c1152G→A
SCN1A	Exon 9	c1183G→C
SCN1A	Exon 9	c1207T→C
SCN1A	Exon 9	c1237T→A
SCN1A	Exon 9	c1265T→A
SCN1A	Exon 21	c4219C→T
SCN1A	Exon 26	c5339T→C
SCN1A	Exon 26	c5674C→T
SCN1B	Exon 3	c254G→A
SCN2A	Exon 6A	c668G→A
SCN2A	Exon 16	c2674G→A
SCN2A	Exon 17	c3007C→A
SCN2A	Exon 19	c3598A→G
SCN2A	Exon 20	c3956G→A
SCN2A	Exon 12	c1785T→C
SCN2A	Exon 27	c4919T→A
SCN1A	Intron 9	IVS9-1G→A
SCN1A	Intron 23	IVS23+33G→A
SCN2A	Intron 7	IVS7+61T→A
SCN2A	Intron 19	IVS19-55A→G
SCN2A	Intron 22	IVS22-31A→G
SCN2A	Intron 2	IVS2-28G→A
SCN2A	Intron 8	IVS8-3T→C
SCN2A	Intron 11	IVS11+49A→G
SCN2A	Intron 11	IVS11-16C→T

SCN2A	Intron 17	IVS17-71C→T
SCN2A	Intron 17	IVS17-74delG
SCN2A	Intron 17	IVS17-74insG
CHRNA5	Exon 4	c400G→A
CHRNA2	Exon 4	c373G→A
CHRNA3	Exon 2	c110G→A
CHRNA2	Exon 4	c351C→T
CHRNA2	Exon 5	c771C→T
CHRNA3	Exon 2	c159A→G
CHRNA3	Exon 4	c291G→A
CHRNA3	Exon 4	c345G→A
CHRNA2	Intron 3	IVS3-16C→T
CHRNA3	Intron 3	IVS3-5T→C
CHRNA3	Intron 4	IVS4+8G→C
KCNQ2	Exon 1	c204-c205insC
KCNQ2	Exon 1	c1A→G
KCNQ2	Exon 1	c2T→C
KCNQ2	Exon 8	c1057C→G
KCNQ2	Exon 11	c1288C→T
KCNQ2	Exon 14	c1710A→T
KCNQ2	Exon 15	c1856T→G
KCNQ2	Intron 9	IVS9+(46-48)delCCT
KCNQ3	Intron 11	IVS11+43G→A
KCNQ3	Intron 12	IVS12+29G→A
GABRB1	Exon 5	c508C→T
GABRB1	Exon 9	c1329G→A
GABRB1	Exon 8	c975C→T
GABRG3	Exon 8	c995T→C
GABRA1	5′ UTR	c-142A→G
GABRA1	5′ UTR	c-31C→T
GABRA2	3′ UTR	c1615G→A
GABRA5	5′ UTR	c-271G→C
GABRA5	5′ UTR	c-228A→G
GABRA5	5′ UTR	c-149G→C
GABRB2	5′ UTR	c-159C→T
GABRB2	3′ UTR	c1749C→T
GABRPi	5′ UTR	c-101C→T
GABRB1	Intron 1	IVS1+24T→G
GABRB1	Intron 6	IVS6+72T→G
GABRB1	Intron 7	IVS7-34A→G
GABRB3	Intron 1	IVS1-14C→T
GABRB3	Intron 7	IVS7+58delAA
GABRD	Intron 6	IVS6+132insC
GABRD	Intron 6	IVS6+130insC
GABRD	Intron 6	IVS6+73delCGCGCCCACCGCCCCTTCCGCG
GABRG3	Intron 8	IVS8-102C→T

has occurred.

9. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in claim 8 wherein a cDNA derived therefrom comprises the sequence set forth in one of SEQ ID NOS: 1-72.

10. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in claim 8 wherein a cDNA derived therefrom has the sequence set forth in one of SEQ ID NOS: 1-72.

11. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in any one of claims 8 to 10, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype.

12. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in any one of claims 8 to 10, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness.

13. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in any one of

claims 8 to 10, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.

14. An isolated nucleic acid molecule encoding a mutant or variant ion channel subunit as claimed in any one of claims 8 to 10, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness, when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.

15. An isolated nucleic acid molecule comprising any one of the nucleotide sequences set forth in SEQ ID NOS: 1-72.

16. An isolated nucleic acid molecule consisting of any one of the nucleotide sequences set forth in SEQ ID NOS: 1-72.

17. An isolated nucleic acid molecule encoding a mutant KCNQ2 subunit, wherein the mutation event has occurred in the C-terminal domain of the KCNQ2 subunit and leads to a disturbance in the calmodulin binding affinity of the subunit, so as to produce an epilepsy phenotype.

18. An isolated nucleic acid molecule as claimed in claim 17 wherein the mutation event has occurred in exon 8, exon 11, exon 14 or exon 15.

19. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit wherein a mutation event selected from the group consisting of the mutation events set forth in the following Table:

Subunit Gene	Amino Acid Change
SCN1A	R222X
SCN1A	W384X
SCN1A	A395P
SCN1A	F403L
SCN1A	Y413N
SCN1A	V422E
SCN1A	R1407X
SCN1A	M1780T
SCN1A	R1892X
SCN1B	R85H
SCN2A	R223Q
SCN2A	V892I
SCN2A	L1003I
SCN2A	T1200A
SCN2A	R1319Q
CHRNA5	V134I
CHRNA2	A125T
CHRNA3	R37H
KCNQ2	K69fsX119
KCNQ2	M1V
KCNQ2	M1T
KCNQ2	R353G
KCNQ2	R430X
KCNQ2	R570S
KCNQ2	L619R

has occurred.

20. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in claim 19 wherein the polypeptide comprises the amino acid sequence set forth in one of SEQ ID NOS: 73-95.

21. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in claim

19 wherein the polypeptide has the amino acid sequence set forth in one of SEQ ID NOS: 73-95.

22. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in any one of claims 19 to 21, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype.

23. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in any one of claims 19 to 21, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness.

24. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in any one of claims 19 to 21, wherein said mutation event disrupts the functioning of an assembled ion channel so as to produce an epilepsy phenotype when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.

25. An isolated polypeptide, said polypeptide being a mutant or variant ion channel subunit as claimed in any one of claims 19 to 21, wherein said mutation event

disrupts the functioning of an assembled ion channel so as to produce one or more disorders associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness and total colour-blindness, when expressed in combination with one or more additional mutations or variations in said ion channel subunit genes.

26. An isolated polypeptide comprising any one of the amino acid sequences set forth in SEQ ID NOS: 73-95.

27. An isolated polypeptide consisting of any one of the amino acid sequences set forth in SEQ ID NOS: 73-95.

28. An isolated polypeptide, said polypeptide being a mutant KCNQ2 subunit, wherein the mutation event has occurred in the C-terminal domain of the KCNQ2 subunit and leads to a disturbance in the calmodulin binding affinity of the subunit, so as to produce an epilepsy phenotype.

29. An isolated polypeptide complex, said polypeptide complex being an assembled mammalian ion channel including an ion channel subunit comprising a polypeptide as defined in any one of claims 19 to 28.

30. An expression vector comprising a nucleic acid molecule as claimed in any one of claims 8 to 18.

31. A cell comprising at least one expression vector as claimed in claim 30.

32. A cell as claimed in claim 31 comprising two or more expression vectors.

33. A cell comprising at least one ion channel type, wherein the or each ion channel type incorporates at least one mutant polypeptide as claimed in any one claims 19 to 28.

34. A cell as claimed in claim 33 comprising ion channels that incorporate two or more mutant polypeptides.

35. A cell as claimed in claim 33 comprising two or more ion channel types each incorporating one or more mutant polypeptides.

36. A method of preparing a polypeptide, comprising the steps of:

(1) culturing cells as claimed in any one of claims 31 to 35 under conditions effective for polypeptide production; and

(2) harvesting the polypeptide.

37. A polypeptide prepared by the method of claim 36.

38. An antibody which is immunologically reactive with an isolated polypeptide as claimed in any one of claims 19 to 28 or claim 37, or an isolated polypeptide complex as claimed in claim 29.

39. An antibody as claimed in claim 38 which is selected from the group consisting of a monoclonal antibody, a humanised antibody, a chimeric antibody or an antibody fragment including a Fab fragment, (Fab')2 fragment, Fv

fragment, single chain antibodies and single domain antibodies.

40. A method of treating epilepsy comprising administering an antibody as claimed in either one of claims 38 or 39 to a subject in need of such treatment.

41. The use of an antibody, as claimed in either one of claims 38 or 39, in the manufacture of a medicament for the treatment of epilepsy.

42. A method of treating a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness, comprising administering an antibody as claimed in either one of claims 38 or 39 to a subject in need of such treatment.

43. The use of an antibody, as claimed in either one of claims 38 or 39, in the manufacture of a medicament for the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease,

hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

44. A method of treating epilepsy comprising administering a selective agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28 to a subject in need of such treatment.

45. The use of a selective agonist, antagonist or modulator of an ion channel when it has undergone a mutation event as defined in any one of claims 19 to 28 in the manufacture of a medicament for the treatment of epilepsy.

46. A method of treating a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness, comprising administering a selective agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28 to a subject in need of such treatment.

47. The use of a selective agonist, antagonist or modulator of an ion channel when it has undergone a mutation event as claimed in any one of claims 19 to 28 in the manufacture of a medicament for the treatment of a

disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

48. A method of treating epilepsy comprising administering an isolated DNA molecule which is the complement (antisense) of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, to a subject in need of such treatment.

49. The use of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in the manufacture of a medicament for the treatment of epilepsy.

50. A method of treating a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic

fibrosis, congenital stationary night blindness or total colour-blindness, comprising administering an isolated DNA molecule which is the complement (antisense) of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, to a subject in need of such treatment.

51. The use of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in the manufacture of a medicament for the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

52. A method of treating epilepsy comprising administering an antibody, as claimed in either one of claims 38 or 39, administration of an agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28, or administration of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one

of claims 8 to 18, in combination with administration of the wild-type ion channel subunit, to a subject in need of such treatment.

53. The use of an antibody, as claimed in claims 38 or 39, use of an agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28, or use of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in combination with the use of the wild-type ion channel subunit, in the manufacture of a medicament for the treatment of epilepsy.

54. A method of treating a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness, comprising administering an antibody, as claimed in either one of claims 38 or 39, administration of an agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28, or administration of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in

combination with administration of the wild-type ion channel subunit, to a subject in need of such treatment.

55. The use of an antibody, as claimed in claims 387 or 39, use of an agonist, antagonist or modulator of an ion channel when it has undergone a mutation event or combination of events as defined in any one of claims 19 to 28, or use of a DNA molecule which is the complement of a nucleic acid molecule as claimed in any one of claims 8 to 18 and which encodes an RNA molecule that hybridizes with the mRNA encoded by a nucleic acid molecule as claimed in any one of claims 8 to 18, in combination with the use of the wild-type ion channel subunit, in the manufacture of a medicament for the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

56. Use of a nucleic acid molecule as claimed in any one of claims 8 to 18 for the screening of candidate pharmaceutical agents.

57. Use of a nucleic acid molecule as claimed in any one of claims 8 to 18 for the screening of candidate pharmaceutical agents useful for the treatment of epilepsy.

58. Use of a nucleic acid molecule as claimed in any one of claims 8 to 18 for the screening of candidate

pharmaceutical agents useful for the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

59. Use of a polypeptide as claimed in any one of claims 19 to 28 or claim 37, or a polypeptide complex as claimed in claim 29 for the screening of candidate pharmaceutical agents.

60. Use of a polypeptide as claimed in any one of claims 19 to 28 or claim 37, or a polypeptide complex as claimed in claim 29 for the screening of candidate pharmaceutical agents useful for the treatment of epilepsy.

61. Use of a polypeptide as claimed in any one of claims 19 to 28 or claim 37, or a polypeptide complex as claimed in claim 29 for the screening of candidate pharmaceutical agents useful for the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic

fibrosis, congenital stationary night blindness or total colour-blindness.

62. Use of a cell as claimed in any one of claims 31 to 35 for the screening of candidate pharmaceutical agents.

63. Use of a cell as claimed in any one of claims 31 to 35 for the screening of candidate pharmaceutical agents useful for the treatment of epilepsy.

64. Use of a cell as claimed in any one of claims 31 to 35 for the screening of candidate pharmaceutical agents useful for the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

65. A compound when identified through a use as claimed in any one of claims 56 to 64.

66. A pharmaceutical composition comprising a compound as claimed in claim 65 and a pharmaceutically acceptable carrier.

67. A genetically modified non-human animal comprising an isolated nucleic acid molecule as claimed in any one of claims 8 to 18.

68. A genetically modified, non-human animal which comprises two or more isolated nucleic acid molecules as claimed in any one of claims 8 to 18.

69. A genetically modified non-human animal as claimed in either one of claims 67 or 68 in which the animal is selected from the group consisting of rats, mice, hamsters, guinea pigs, rabbits, dogs, cats, goats, sheep, pigs and non-human primates such as monkeys and chimpanzees.

70. A method of producing a non-human transgenic animal comprising a combination of two or more ion channel mutations, comprising the steps of:

(1) creating a non-human transgenic animal comprising a first nucleic acid molecule as claimed in any one of claims 8 to 18;

(2) creating one or more additional non-human, transgenic animals comprising a second nucleic acid molecule as claimed in any one of claims 8 to 18; and

(3) conducting mating combinations so as to produce progeny containing combinations of two or more ion channel mutations which effectively mimic combinations of ion channel mutations responsible for human disease.

71. A non-human, transgenic animal produced by the process of claim 70.

72. The use of a genetically modified non-human animal as claimed in any one of claims 67 to 69 or a non-human transgenic animal as claimed in claim 71 in the screening of candidate pharmaceutical compounds.

73. The use of a genetically modified non-human animal as claimed in any one of claims 67 to 69 or a non-human

transgenic animal as claimed in claim 71 in the screening of candidate pharmaceutical compounds useful in the treatment of epilepsy.

74. The use of a genetically modified non-human animal as claimed in any one of claims 67 to 69 or a non-human transgenic animal as claimed in claim 71 in the screening of candidate pharmaceutical compounds useful in the treatment of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

75. The use of an isolated nucleic acid molecule as claimed in any one of claims 8 to 18 for the diagnosis or prognosis of epilepsy.

76. The use of an isolated nucleic acid molecule as claimed in any one of claims 8 to 18 for the diagnosis or prognosis of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis,

congenital stationary night blindness or total colour-blindness.

77. The use of a polypeptide as defined in any one of claims 19 to 28 or claim 37, or polypeptide complex as claimed in claim 29 in the diagnosis or prognosis of epilepsy.

78. The use of a polypeptide as defined in any one of claims 19 to 28 or claim 37, or polypeptide complex as claimed in claim 29 in the diagnosis or prognosis of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

79. The use of an antibody as claimed in either one of claims 38 or 39 in the diagnosis or prognosis of epilepsy.

80. The use of an antibody as claimed in either one of claims 38 or 39 in the diagnosis or prognosis of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of

infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness.

81. A method for the diagnosis or prognosis of epilepsy comprising the steps of:

(1) obtaining DNA from a subject; and

(2) comparing the DNA of one or more subunits of ion channels from said subject to the DNA of the corresponding native subunits;

wherein identification of one or more DNA molecules as claimed in any one of claims 8 to 18 is an indication of epilepsy, or a predisposition thereto.

82. A method for the diagnosis or prognosis of a disorder associated with ion channel dysfunction, including but not restricted to, hyper- or hypo-kalemic periodic paralysis, myotonias, malignant hyperthermia, myasthenia, cardiac arrhythmias, episodic ataxia, migraine, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia, anxiety, depression, phobic obsessive symptoms, neuropathic pain, inflammatory pain, chronic/acute pain, Bartter's syndrome, polycystic kidney disease, Dent's disease, hyperinsulinemic hypoglycemia of infancy, cystic fibrosis, congenital stationary night blindness or total colour-blindness, comprising the steps of:

(1) obtaining DNA from a subject; and

(2) comparing the DNA of one or more subunits of ion channels from said subject to the DNA of the corresponding native subunits;

wherein identification of one or more DNA molecules as claimed in any one of claims 8 to 18 is an indication of the disorder, or a predisposition thereto.

83. A method as claimed in either one of claims 81 or 82 wherein each DNA fragment is sequenced and the sequences compared.

84. A method as claimed in either one of claims 81 or 82 wherein the DNA fragments are subjected to restriction enzyme analysis.

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85. A method as claimed in either one of claims 81 or 82 wherein the DNA fragments are subjected to SSCP analysis.